

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANT: Nakamura, et al.  
SERIAL NUMBER: 10/788,847 EXAMINER : Not Yet Assigned  
FILING DATE: February 27, 2004 ART UNIT : Not Yet Assigned  
FOR: GENE AND PROTEIN RELATING TO HEPATOCELLULAR  
CARCINOMA AND METHODS OF USE THEREOF

**Mail Stop IDS**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**TRANSMITTAL LETTER**

Transmitted herewith for filing in the present application are the following documents:

1. Information Disclosure Statement (2 pages), in duplicate;
2. Modified Form 1449/PTO (3 pages), in duplicate;
3. Copies of Cited References: B1-B5; C1-C56; and
4. Return Postcard.

If the enclosed papers are considered incomplete, the Mail Room and/or the Application Branch is respectfully requested to contact the undersigned at (617) 542-6000, Boston, Massachusetts.

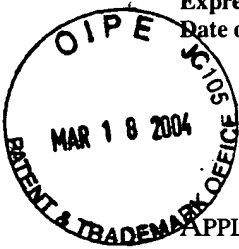
The Commissioner is authorized to charge any fees that may be due, or to credit any overpayment, to the undersigned's account, Deposit Account No. 50-0311 Ref. No. 25371-021 CIP. A duplicate copy of this transmittal letter is enclosed herewith.

Respectfully submitted,

*IA Beattie*

Ingrid A. Beattie, Reg. No. 42,306  
Cynthia A. Kozakiewicz, Reg. No. 42,764  
Attorneys for Applicants  
MINTZ, LEVIN, COHN, FERRIS,  
GLOVSKY and POPEO, P.C.  
One Financial Center  
Boston, Massachusetts 02111  
Tel: (617) 542-6000  
Fax: (617) 542-2241  
Customer No. 30623

Dated: March 18, 2004



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANT: Nakamura, et al.  
SERIAL NUMBER: 10/788,847 EXAMINER : Not Yet Assigned  
FILING DATE: February 27, 2004 ART UNIT : Not Yet Assigned  
FOR: GENE AND PROTEIN RELATING TO HEPATOCELLULAR  
CARCINOMA AND METHODS OF USE THEREOF

**MAIL STOP IDS**

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

**INFORMATION DISCLOSURE STATEMENT**

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, Applicants hereby make of record the documents listed on the attached modified Form PTO-1449, as well as copies of the listed documents.

This Information Disclosure Statement is being filed before the mailing date of a first Office Action based on the merits in the above-identified case. Accordingly, no fee or certification is believed required.

It is respectfully requested that the Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims, and sign the enclosed form PTO-1449 to evidence that the cited information has been fully considered by the Patent and Trademark Office during the examination of this application.

By submitting this Information Disclosure Statement, the Applicants make no representation that: (1) a search has been performed, of the extent of any search performed, or that more relevant information does not exist; (2) the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. §1.56(b); and (3) the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

APPLICANT: Nakamura, et al.  
U.S.S.N.: 10/788,847

Notwithstanding any statements by the Applicants, the Examiner is urged to form his/her own conclusion regarding the relevance of the cited information. An early and favorable action is hereby requested.

Please charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 25371-021 CIP.

Respectfully submitted,



Ingrid A. Beattie, Reg. No. 42,306  
Cynthia A. Kozakiewicz, Reg. No. 42,764  
Attorneys for Applicants  
MINTZ, LEVIN, COHN, FERRIS,  
GLOVSKY and POPEO, P.C.  
One Financial Center  
Boston, Massachusetts 02111  
Tel: (617) 542-6000  
Fax: (617) 542-2241  
Customer No. 30623

Dated: March 18, 2004

TRA 1897921v1

Please type a plus sign (+) in this box



|  |                        |                   |
|--|------------------------|-------------------|
| <b>Modified Form 1449/PTO</b><br><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br>(use as many sheets as necessary) | Application Number     | 10/788,847        |
|  | Filing Date            | February 27, 2004 |
|  | First Named Inventor   | Nakamura          |
|  | Group Art Unit         | Not Yet Assigned  |
|  | Examiner Name          | Not Yet Assigned  |
|  | Attorney Docket Number | 25371-021 CIP     |

**U.S. PATENT DOCUMENTS**

| Exam Initials | Cite No. | U.S. Patent Document No. | Issue Date | Name of Patentee(s) or Applicant(s) | Class | Sub Class | Filing Date If Appropriate |
|---------------|----------|--------------------------|------------|-------------------------------------|-------|-----------|----------------------------|
|               |          |                          |            |                                     |       |           |                            |

**U.S. PUBLISHED APPLICATION DOCUMENTS**

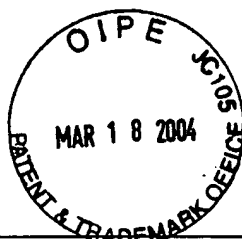
| Exam Initials | Cite No. | U.S. Published Application No. | Published Date | Name of Patentee(s) or Applicant(s) | Class | Sub Class | Filing Date If Appropriate |
|---------------|----------|--------------------------------|----------------|-------------------------------------|-------|-----------|----------------------------|
|               |          |                                |                |                                     |       |           |                            |

**FOREIGN PATENT DOCUMENTS**

| Exam Initials | Cite No. | Foreign Patent Document Office Number | Name of Patentee(s) or Applicant(s)      | Date of Publication | Translation Yes No |
|---------------|----------|---------------------------------------|--|---------------------|--------------------|
|               | B1       | WO 99/39200                           | THOMAS JEFFERSON UNIVERSITY              | 08/05/99            |                    |
|               | B2       | WO 00/17355                           | INCYTE PHARMACEUTICALS, INC.             | 03/30/00            |                    |
|               | B3       | WO 00/44900                           | INCYTE PHARMACEUTICALS, INC.             | 08/03/00            |                    |
|               | B4       | WO 03/027143 A2&A3                    | THE PRESIDENT OF THE UNIVERSITY OF TOKYO | 04/03/03            |                    |
|               | B5       | WO 03/027322 A2&A3                    | THE PRESIDENT OF THE UNIVERSITY OF TOKYO | 04/03/03            |                    |

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

| Exam Initials | Cite No. | Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc. |
|---------------|----------|--|
|               | C1       | Ansieau, et al., <i>J. Biol. Chem.</i> , 277(7):4906-4910 (2002).                  |
|               | C2       | Aratani, et al., <i>Mol. Cell. Biol.</i> , 21(14):4460-4469 (2001).                |
|               | C3       | Brummelkamp, et al., <i>Science</i> , 296(5567):550-553 (2002).                    |
|               | C4       | Cerione, et al., <i>Curr. Opin. Cell Biol.</i> , 8(2):216-222 (1996).              |
|               | C5       | Chardin, et al., <i>Nature</i> , 384(6608):481-484 (1996).                         |
|               | C6       | Choi, et al., <i>Cancer</i> , 79(10):1879-1883 (1997).                             |
|               | C7       | Cukierman, et al., <i>Science</i> , 270(5244):1999-2002 (1995).                    |
|               | C8       | DATABASE EMBL Accession No. AK000206, February 22, 2000.                           |
|               | C9       | DATABASE EMBL Accession No. BG773806, May 16, 2001.                                |
|               | C10      | Delwel, et al., <i>Mol. Cell. Biol.</i> , 13(7):4291-4300 (1993).                  |
|               | C11      | Elbashir, et al., <i>Nature</i> , 411(6836):494-498 (2001).                        |
|               | C12      | EMBL Accession No. AL557360, February 11, 2001.                                    |
|               | C13      | Fu, et al., <i>J. Virol.</i> , 67(12):6965-6972 (1993).                            |
|               | C14      | Gelmetti, et al., <i>Mol. Cell. Biol.</i> , 18(12):7185-7191 (1998).               |
|               | C15      | Ghanem, et al., <i>Cancer</i> , 92(12):3120-3129 (2001).                           |



| OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS |          |  |
|---|----------|--|
| Exam Initials                                     | Cite No. | Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.   |
|   | C16      | Golub, et al., <i>Science</i> , 286(5439):531-537 (1999).  |
|   | C17      | Gross, et al., <i>EMBO J.</i> , 15(8):1961-1870 (1996).  |
|   | C18      | Hamamoto, et al., <i>Proceedings of the Am. Assoc. for Cancer Res. Annual</i> , 43:13(#63), and English translation, (2002).                           |
|   | C19      | Hamamoto, et al., <i>94<sup>th</sup> Annual Mtg. Of the Am. Assoc. for Cancer Res.</i> , 44:54(#236), and English translation, (2003).                 |
|   | C20      | Hamamoto, et al., <i>94<sup>th</sup> Annual Mtg. Of the Am. Assoc. for Cancer Res.</i> , 44(Second Edition):47(#236), and English translation, (2003). |
|   | C21      | Hamamoto, et al., <i>Jpn. J. Cancer Res.</i> , 92(Supplement):117(#208), and English translation, (2001).  |
|   | C22      | Hamamoto, et al., <i>Jpn. J. Cancer Res.</i> , 93(Supplement):78(#2032), and English translation, (2002).  |
|   | C23      | Hamamoto, et al., <i>Jpn. J. Cancer Res.</i> , 286(#3339-OP), and English translation, (2003).   |
|   | C24      | Hamamoto, et al., <i>Jpn Assoc. Mol. Target Ther. Cancer</i> , 36(#SY-1), and English translation, (2002).   |
|   | C25      | Hammond, et al., <i>Nature</i> , 404(6775):293-296 (2000).   |
|   | C26      | Hannon, et al., <i>Nature</i> , 418(6894):244-251 (2002).  |
|   | C27      | Herbst, et al., <i>Cancer</i> , 94(5):1593-1611 (2002).  |
|   | C28      | Hermouet, et al., <i>Proc. Natl. Acad. Sci. USA</i> , 88(23):10455-10459 (1991).   |
|   | C29      | Ito, et al., <i>Br. J. Cancer</i> , 84(10):1377-1383 (2001).   |
|   | C30      | Jackson, et al., <i>Trends Biochem. Sci.</i> , 25(10):489-495 (2000).  |
|   | C31      | Kato, et al., <i>Jpn. J. Cancer Res.</i> , 93(Supplement):78(2033), and English translation, (2002).   |
|   | C32      | Kibar, et al., <i>Nat. Genet.</i> , 28(3):251-255 (2001).  |
|   | C33      | Lüking, et al., <i>Crit. Rev. Biochem. Mol. Biol.</i> , 33(4):259-296 (1998).  |
|   | C34      | Lutterbach, et al., <i>Mol. Cell. Biol.</i> , 18(12):7176-7184 (1998).   |
|   | C35      | Lyons, et al., <i>Science</i> , 249(4969):655-659 (1990).  |
|   | C36      | Masselink, et al., <i>Oncogene</i> , 19(12):1538-1546 (2000).  |
|   | C37      | Mendelsohn, et al., <i>Oncogene</i> , 19(56):6550-6565 (2000).   |
|   | C38      | Miyagishi, et al., <i>Nat. Biotechnol.</i> , 19:497-500 (2002).  |
|   | C39      | Miyaki, et al., <i>Int. J. Cancer</i> , 85(4):518-522 (2000).  |
|   | C40      | Mochizuki, et al., <i>Gene</i> , 181(1-2):39-43 (1996).  |
|   | C41      | Moss, et al., <i>J. Biol. Chem.</i> , 270(21):12327-12330 (1995).  |
|   | C42      | Nakajima, et al., <i>Cell</i> , 90(6):1107-1112 (1997).  |
|   | C43      | Okabe, et al., <i>Cancer Res.</i> , 61(5):2129-2137 (2001).  |
|   | C44      | Pace, et al., <i>Proc. Natl. Acad. Sci. USA</i> , 88(16):7031-7035 (1991).   |
|   | C45      | Perou, et al., <i>Nature</i> , 406(6797):747-752 (200).  |
|   | C46      | Randazzo, et al., <i>Proc. Natl. Acad. Sci. USA</i> , 97(8):4011-4016 (2000).  |
|   | C47      | Sharp, P.A., <i>Genes Dev.</i> , 13(2):139-141 (1999).   |
|   | C48      | Tanaka, et al., <i>Biochim. Biophys. Acta</i> , 1536(1):1-12 (2001).   |
|   | C49      | Tang, et al., <i>Mol. Cell. Biol.</i> , 19(5):3540-3550 (1999).  |
|   | C50      | Tanner, et al., <i>Mol. Cell</i> , 8(2):251-262 (2001).  |
|   | C51      | von Marschall, et al., <i>Gut</i> , 48(1):87-96 (2001).  |

Express Mail Label: EV 392154295 US  
Date of Deposit: March 18, 2004



Page 3 of 3  
Attorney Docket No.: 25371-021 CIP

| OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS |          |   |
|---|----------|---|
| Exam Initials                                     | Cite No. | Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.                            |
|   | C52      | Westermarck, et al., <i>EMBO J.</i> , 21(3):451-460 (2002).   |
|   | C53      | Wolff, et al., <i>Development</i> , 125(6):1149-1159 (1998).  |
|   | C54      | Yagyu, et al., <i>Jpn. J. Cancer Res.</i> , 92(Supplement):118(209), and <b>English translation</b> , (2001). |
|   | C55      | Yagyu, et al., <i>Int. J. Oncol.</i> , 20(6):1173-1178 (2002).  |
|   | C56      | Ying, et al., <i>Biochem. Biophys. Res. Commun.</i> , 286(2):394-400 (2001).                                  |

A copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. \_\_\_\_\_, filed \_\_\_\_\_, and relied upon for an earlier filing date under 35 U.S.C. §120 (continuation, continuation-in-part, and divisional applications).

|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

TRA 1897706v1